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NAMRU-D's mission is to maximize warfighter performance and survivability through world-class aeromedical and environmental health research by delivering solutions to the field, the Fleet, and for the future.

Research Areas

Aeromedical Directorate

The Aeromedical Directorate conducts aerospace-relevant basic and applied research in the biomedical and behavioral sciences. Key areas of investigation include: spatial disorientation (SD), situational awareness, motion sickness, unusual acceleration environments, effects of altitude, sustained operations and fatigue, personnel selection, and visual and auditory sciences. Research efforts focus on the transition of products from our basic and applied research base to Navy Medicine, Naval Aviation, and other governmental and civilian customers. Recent and anticipated transitions include: validated aviation selection tests, novel training media to reduce SD mishaps, and new medications for motion sickness. Our lab boasts a unique set of man-rated acceleration devices used by NAMRU-D researchers and international visiting scientists to maintain a technology base critical to Naval Aviation and other federal and non-federal aerospace customers.

Environmental Health Effects Directorate

The Environmental Health Effects Directorate conducts basic and applied research to assess the toxicity of chemicals and materials used in military operations that may affect our military and civilian populations. NAMRU-D has the capability to study toxic effects of materials using both *in vitro* and *in vivo* systems and then use the data to assess risk using *in silico* (modeling) approaches. Our *in vitro* approaches provide key data on the cytotoxicity, mutagenicity, genotoxicity, and the mechanism of toxic action of these materials. We use animal systems to examine the toxicities of materials via various routes of exposure. Our inhalation capabilities are extensive, allowing for exposures to gases and vapors, aerosols, particulates, and nanoparticles, using both whole-body and nose-only inhalation chambers. Thus, we have the ability to assess the toxicities of chemicals and materials via various routes of exposure at the molecular, cellular, organ, and whole body levels. The results from these efforts have led to state-of-the-science health protective exposure standards for our military and civilian populations.

The Highlights of Recent Research Efforts, Ongoing Projects, and Future Projects at NAMRU-D

Aeromedical Directorate

Aviation Selection

Personnel selection testing is used in aviation to identify pilot candidates who have high likelihood of success in flight training and operations. NAMRU-D's Aeromedical Research Lab has a 70 year history of research in this area. NAMRU-D researchers recently validated the Performance Based Measurement (PBM) test battery, which will be fielded for use in the selection of Navy and USMC student pilots and flight officers later this year. Current efforts are focused on the development and validation of tests for selecting operators of unmanned aircraft systems, the next frontier in Naval Aviation.

Hypoxia Research

Since FY-2000 there have been four hypoxia related Class A flight mishaps, costing the Department of Defense (DoD) four lives and over $300 million in assets. A 2010 survey of Naval aviators also indicates that the problem is grossly under-reported. NAMRU-D houses a state-of-the-science hypoxia research program that focuses on studying hypoxia's negative effects on human performance, the time course of those effects, and early detection via physiological sensors. The end goals are to increase the aviation community's understanding of hypoxia and to reduce hypoxia related mishaps within the Fleet.

Motion Sickness Countermeasures

Motion sickness (MS) is a significant problem across a wide range of operational environments. A current NAMRU-D study is investigating the efficacy of a low-dose, fine particulate intranasal scopolamine spray for treatment of MS. If, as hypothesized, this formulation exhibits negligible side effects, rapid bioavailability, and greater efficacy than traditional formulations, then DoD will have a MS countermeasure that is highly effective, safe, and easy to administer, improving mission effectiveness across a variety of operational environments.

Environmental Health Effects Directorate

Mixed Gender Crews in Submarine Atmospheres

US Navy exposure limits for contaminants found in submarine atmospheres were established for male crew members only. Female crew members will soon be reporting aboard submarines and the health of all crew members must be protected. NAMRU-D is conducting studies in laboratory animals to assess the reproductive and developmental hazards posed by certain key atmospheric contaminants found aboard submarines. The results from these studies will indicate whether the existing standards for the chemicals under study require updating.

Toxicities of Burn Pit Emissions

NAMRU-D is assessing the potential health risks to deployed personnel from the inhalation of contaminants emitted from the open burning of solid waste. This project will: (1) characterize "burn pit" emissions produced from the combustion of in-theater solid waste; (2) assess the toxicity and inflammatory impacts of the contaminant smoke utilizing human airway tissue cultures; (3) determine adverse pulmonary health effects by performing rodent inhalation exposure studies; and, (4) identify potential exposure biomarkers.

Particulate Matter and Traumatic Brain Injury

Researchers are actively involved in developing an animal model that mimics environmental exposures of personnel to blast trauma, examining responses in conjunction with sand dust particulate exposure, and analyzing the potential mechanisms of brain injury. These research efforts include the study of both molecular-genomic responses and neurocognitive and behavioral performance associated with blast and sand dust exposure. This information will be used to identify biomarkers and novel strategies for preventing or mitigating blast-related trauma.

Aeromedical Directorate (cont.)

Fatigue Measurement, Management, and Mitigation

Fatigue is cited as the number one aeromedical factor implicated in Naval Aviation mishaps. Dynamic operational conditions call for fatigue measurement, management, and mitigation options. NAMRU-D fatigue research efforts are addressing all three angles. On-going protocols are focused on: 1) *measurement* of individual differences in response to fatigue under realistic restricted-sleep conditions, 2) *management* in a field test of a quick, non-invasive, fatigue-detection tool, and 3) *mitigation* of fatigue effects using novel pharmacologic and non-pharmacologic countermeasures. By refining existing fatigue prediction and scheduling tools, testing improved pharmacologic alertness aids, and evaluating fatigue-inoculating cognitive training programs, NAMRU-D is on the forefront of increasing Fleet effectiveness, efficiency, and safety.

Unmanned Aircraft Systems (UAS) Human Factors

As the use of UAS within the DoD continues to grow rapidly, critical S&T gaps remain in such areas as UAS manning, personnel selection and training, distributed crew situation awareness, and common control station design. NAMRU-D is addressing these questions through efforts such as the Cross-Platform UAS Job Task Analysis. This joint effort between NAMRU-D and NAVAIR is building a solid understanding of UAS crewmembers' jobs by identifying and analyzing the tasks performed by crews of seven different USN/USMC UAS platforms. The results will be used to optimize UAS manning levels, selection and training procedures, and interface design for the Fleet, ultimately improving operator performance and mission effectiveness.

Spatial Disorientation

The Naval Safety Center cites Spatial Disorientation (SD) as the principal contributing factor in Class A aviation mishaps. While SD has been traditionally and primarily attributed to vestibular cues, NAMRU-D researchers are taking a novel approach that considers the role played by visual cues, and their resulting cockpit spatial strategies. One new study is using NAMRU-D's unique Visual Vestibular Sphere Device and dense-array EEG technology to image the neural processes that contribute to cognitive formulation of human spatial strategies. Findings from this research are expected to lead to reduced spatial disorientation and motion sickness in the Fleet, more effective flight simulation for training, and improved mishap analysis.

Capabilities

NAMRU-D research capabilities in the visual, vestibular, and cognitive sciences are supported by a unique collection of state-of-the-science equipment and research devices. NAMRU-D's human-rated motion platforms include the **Disorientation Research Device (DRD)**, the **Visual Vestibular Sphere Device (VVSD)**, **the Vertical Linear Accelerator (VLA)**, and the **Neuro-Otologic Test Center (NOTC)**. Each device is capable of unique motion profiles, affording independent control of visual and vestibular stimuli to isolate sensory interactions associated with spatial disorientation and motion sickness. NAMRU-D's hypoxia program is supported by a lab suite capable of running up to six **Reduced Oxygen Breathing Devices (ROBD's)**, each of which can simulate altitude exposures at up to 34k' under normobaric conditions. NAMRU-D facilities also house a vision suite containing a full array of **ophthalmic equipment** for evaluating vision performance prior to and during protocols. This unique assortment of capabilities enables NAMRU-D to transition validated knowledge and effective technologies to the fleet that will mitigate and prevent leading factors associated with aeromedical mishaps.

Environmental Health (cont.)

In Vivo Toxicity of Jet Fuel

As the military seeks to employ recently developed synthetic and biologically-produced alternatives to petroleum-based jet fuels, addressing potential health problems due to routine exposure to these fuels is important in qualifying the fuels for military use. Sub-chronic 90-day inhalation toxicity studies in rats are being performed to identify potential adverse physiological, biological and genotoxic effects of these novel jet fuels. These studies will help establish safe exposure guidelines for use of this important new class of renewable jet fuel alternatives.

In Vitro Screening of Fuels

The DoD has accelerated research on advancing alternative and bio-fuel generation, approval and use. The US Navy and Air Force have set goals of using 50% alternative fuels by 2020 and 2016, respectively. In addition to performance based testing, new, previously untested, fuels will need to be evaluated for potential toxicological effects. NAMRU-D researchers are developing and validating *in vitro* methods for rapidly and cost-effectively screening alternative fuels. These methods include primary skin cells, a 3-dimensional human skin model (dermal) and various lung models (i.e., inhalation) to assess cytotoxicity as well as inflammatory and irritancy endpoints.

Immunotoxicity of Tungstate

At military firing ranges, spent tungsten alloy munitions can be solubilized by rain water and enter the ground water where military personnel and their families may be at risk of exposure. Researchers at NAMRU-D are investigating the effects of tungstate on the immune response to determine if there is a significant risk to exposed individuals. Previous work at NAMRU-D has shown that tungstate exposure results in suppression of the host immune response. For example, after thermal trauma and infection, host mortality is increased due to tungstate exposure. In a severe allergic hypersensitivity model the allergy induced inflammation is reduced. Current investigations into tungstate include the development of a physiologically based pharmacokinetic model of tungstate distribution in the body, as well as an examination of the effects of the tungstate polymer metatungstate on immune responses in mice.

Cancer and Non-Cancer Risk of RDX

RDX is a common explosive used in military operations since WWII and its use has led to contamination of water and soil in and around military bases. The existing exposure standards for non-cancer and cancer health effects are outdated, so new, state-of-the-scientific evaluations are required. NAMRU-D is developing physiologically based pharmacokinetic (PBPK) models for RDX kinetics in rats, mice and humans to allow for these updated assessments. The use of internal target tissue doses from the PBPK models has resulted in a recommended exposure standard for noncancer effects that is both health protective and higher than those derived previously. These updated standards will allow substantial savings to DoD facilities that require remediation of water and soil in and around military bases.

Mechanisms of Toxicities

Toxic load models are mathematical calculations that are used to estimate consequences (e.g. casualties) from exposure of humans to toxic materials, such as civilians exposed to toxic industrial chemicals, or military personnel exposed to chemical warfare agents. NAMRU-D will test the validity of the toxic load models for extrapolation from constant exposures to time-varying exposures by comparing outcomes from rat studies with standard (constant) profiles with outcomes from studies where rats are exposed to time varying concentrations. This study will use, as a test case, hydrogen cyanide as the agent and lethality as the endpoint. It is expected that the results of this study of hydrogen cyanide would be relevant to the modeling of other industrial chemicals and chemical warfare agents.